REMARKS

Claims 3 – 8, 18, 22, and 24-25 are before the Examiner for consideration.

CLAIM OBJECTIONS

Claims 4 - 8, 18, and 22 have been objected to because they include nucleic acids encoding SEQ ID NOS: 2 or 4. The Examiner has required that these nucleic acids be removed from the claims. Claims 4, 5, 6, 8 and 22 have been objected to because they contain grammatical errors. In particular, the Examiner requests that Applicant insert the word "a" before "DNA sequence" and place the word "and" between the words "enhancers" and "ribosonal binding sights" in claim 4.

In response to this objection, Applicant has amended the pending claims to remove SEQ ID NOS: 2 and 4 from the claims. In addition, Applicant has amended claim 4 to recite "a DNA sequence" and to recite "enhancers and ribosomal binding sites" as suggested by the Examiner. Accordingly, Applicant respectfully requests that this objection be reconsidered and withdrawn.

OBJECTION TO THE SPECIFICATION

The Examiner has objected the specification because it contains two pages labeled as "Page 1". The Examiner states that the translator's comment at the second "Page 1" should be deleted and the remaining pages of the specification be renumbered consecutively.

On Friday, May 16, 2003, Applicant's representative held a brief telephone conversation with the Examiner regarding the present specification. It appears from the conversation that there is a discrepancy in the application that Applicant has of record as being filed in the USPTO and the application that is presently of record in the Examiner's file wrapper. In particular, Applicant has no record of an application containing two pages

labeled as page 1. In response to this objection, Applicant respectfully submits a clean copy of the specification as a courtesy to the Examiner, containing consecutively numbered pages, and respectfully requests that this application be substituted for the specification of record at the USPTO pursuant to MPEP §608.01(q) and that the objection be withdrawn. Alternatively, Applicant respectfully requests that this objection be held in abeyance until the Examiner and Applicant's representative can hold a formal telephone interview on this issue.

REJECTION UNDER 35 U.S.C. § 101

Claim 18 has been rejected under 35 U.S.C. § 101 because the claim recites a "use" without including any steps involved in the process.

In response to this rejection, Applicant has amended claim 18 to recite a method for forming an isoprenoid including the steps of "incorporating the isolated nucleic acid of claim 3 into a genome of a virus, a eukaryote, or a prokaryote to activate isoprenoid biosynthesis, cultivating the virus, eukaryote or prokaryote, and isolating the isoprenoid." Applicant submits that claim 18 as amended recites a proper method claim. Therefore, Applicant respectfully requests that the Examiner reconsider and withdraw this rejection.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 3 - 8, 18 and 22 have been rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. In particular, the Examiner asserts that the specification does not reasonably provide enablement for SEQ ID NO: 6, or for any analog or derivative of SEQ ID NO: 6 not known in the prior art. The Examiner asserts that in view of the unpredictable nature of protein structure function relationships and the assignment in the prior art of a different catalytic activity to gcpE, there is reason to doubt that SEQ ID NO: 6 encodes a

kinase, and it is unpredictable what alterations to SEQ ID NO: 6 would produce kinase activity.

In addition, the Examiner asserts that the specification does not provide enablement for any single promoter that functions in a prokaryote, a eukaryote, and a virus. The Examiner notes that although synthetic promoters exists that will function in both prokaryotes and eukaryotes, there is no evidence in the prior art of record that any promoter functions within a viral particle.

The Examiner concludes that because there is a reason to doubt Applicant's assertion in the specification that SEQ ID NO: 6 encodes a kinase and because neither the prior art of record nor the specification provides or guidance as how to obtain a promoter that is active in a viral particle, one of skill in the art could not make or use the present invention.

With respect to the Examiner's assertion that the specification does not provide enablement for any analog or derivative of SEQ ID NO: 6, Applicant has amended claim 3 to recite an isolated nucleic acid molecule that comprises a sequence that encodes a polypeptide having the amino acid sequence shown in SEQ ID NO: 6 or SEQ ID NO: 6 with conservative amino acid substitutions. Applicant respectfully submits that one of skill in the art would know that a conservative amino acid substitution includes a replacement of one amino acid residue with a different residue having similar biochemical characteristics, such as, for example, the substitution of one amino acid for another amino acid of the same class (e.g. valine for glycine, arginine for lysine, etc.). Such substitutions, which may be a result of the natural degeneracy of the genetic code, are supported in the specification at page 4, lines 7-13. Applicant submits that such conservative substitutions are easily identifiable by those of skill in the art.

With respect to the Examiner's assertion that the specification does not provide enablement for a promoter that functions in a prokaryote, a eukaryote, and a virus, Applicant

has amended claim 5 to recite "a promoter which ensures the formation of an RNA in the intended target tissue or target cells." As amended, claim 5 no longer requires a promoter that functions in a prokaryote, a eukaryote, and a virus.

In view of the above, Applicant submits that the claims as amended are sufficiently enabled and respectfully requests that the Examiner reconsider and withdraw this rejection.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 3 - 8, 18 and 22 have been rejected under 35 U.S.C. § 112, first paragraph as containing subject matter that was described in the specification in such a way as to reasonably convey to one of skill in the art that the inventor had possession of the claimed invention at the time the application was filed.

The Examiner asserts that the claims embrace an analogue of SEQ ID NO: 6 in which any number of amino acids is deleted or replaced and the catalytic function of the polypeptide is retained. The Examiner asserts that that specification discloses a single species of polypeptide (SEQ ID NO: 6). However, Examiner questions whether this polypeptide encodes a kinase as asserted in the specification. The Examiner asserts that the specification fails to provide any relevant identifying characteristics such as a known correlation between structure and function that is common to members of the genus. Thus, the Examiner concludes that one of skill in the art could reasonably conclude that Applicant was not in possession of the claimed invention at the time of filing.

It is known that isoprenoid synthesis can occur through one of two pathways, namely, a mevalonate dependent pathway and an alternative DOXP pathway (also known as the MEP pathway), which is not present in humans. (*See, e.g.*, Fig. 1 of Altincicek et al., *J. Bacteriol.* 183:2411-2416 (2001) and Fig. 1 of the German priority application DE 19923567 (1998) attached hereto for the Examiner's convenience). In addition, Altincicek et al. teach that

although the terminal biosynthetic steps of the DOXP pathway have not been fully elucidated, it has been determined that the gcpE gene isolated from *E. coli* is involved in the DOXP pathway. (*See, e.g.,* Abstract of Altincicek et al.). Further, as described in Altincicek et al., the isolated sequences from *E. coli* (gcpE) can produce isoprenoids via the DOXP pathway. Thus, these sequences have a known function in the DOXP pathway (*e.g.*, producing isoprenoids). It can be concluded from Altincicek et al. that sequences for gcpE/GcpE have an effect on the biosynthesis and amount and control of isoprenoids in any organism that contains the DOXP pathway. The present invention relates to genes and proteins (*i.e.*, GcpE) derived from the parasite *P. falciparum*, which, as indicated above, clearly has a function or is otherwise involved in the DOXP pathway. In particular, the function of the claimed sequence can be seen in its indispensable and credible role in the DOXP pathway for the synthesis of IPP (end product, isoprenoid).

In addition, Applicant wishes to note that genes and proteins (*e.g.*, lytB/LytB), such as are disclosed in PCT/EP01/04637, have recently been identified as being involved in the DOXP pathway. Fig. 1 of the JOCNote attached hereto shows that GcpE (ispG) converts cMEPP to HMBPP (HDMAPP)). (*See* JOCNote, J. Org. Chem. 2002, 67, 5009-5010).

In view of the above, Applicant submits that Applicant had possession of the claimed invention at the time the application was filed and therefore respectfully requests that the Examiner reconsider and withdraw this rejection.

REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 3 - 8, 18 and 22 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. For example, the Examiner asserts that claim 3 and its dependent claims are indefinite because the scope of "analog", "derivative" and "retained" is unclear. The

Examiner also asserts that these claims are indefinite because they recite "the catalytic function" and "the polypeptide" without proper antecedent basis.

Claims 4, 6 and 7 are asserted as being indefinite because the phrase "in particular" makes it unclear whether the limitations following the phrase are part of the claimed invention or if the limitations are optional.

Claim 5 is assertedly indefinite because it recites "the intended target tissue" without antecedent basis.

Claims 6 and 22 are assertedly indefinite because the claims recite "the isoprenoid content" without proper antecedent basis.

Claim 7 is assertedly indefinite because it is unclear what is embraced by the phrase "transgenic systems".

Claim 18 does not include any steps involved in the method/process. Therefore the Examiner asserts that it is unclear what method/process Applicant is intending to encompass.

In response to this rejection, Applicant has amended the claims to correct any improper antecedent basis. In addition, Applicant has removed the phrases "analog or derivative", "in particular", "foreign," and "additional" from the claims. With respect to the Examiner's rejection of claim 7, Applicant has replaced "transgenic systems" with "transgenic viruses, prokaryote, or eukaryotes". With respect to claim 18, Applicant has amended the claim to recite a method for forming an isoprenoid.

In view of the above, Applicant respectfully submits that the claims as amended are sufficiently definite and respectfully requests that the Examiner reconsider and withdraw this rejection.

REJECTION UNDER 35 U.S.C. § 102(b)

Claims 3, 4, 6 - 8 and 18 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Rather et al. In particular, the Examiner asserts that Rather et al. teach an expression construct encoding E. coli gcpE, a transgenic bacterium comprising the construct, and a process for making the bacterium. The Examiner notes that for the purpose of this rejection, he has considered the E. coli gcpE gene to be an analog of SEQ ID NO: 6. The Examiner asserts that the scope of the genus of analog appears to extend to any gcpE protein with catalytic function, and concludes that the claims encompass the nucleic acid disclosed in Rather et al.

In response to this rejection, Applicant submits that Rather et al. do not disclose the isolated nucleic acid as claimed. In particular, Rather et al. do not disclose an isolated nucleic acid molecule that encodes a polypeptide that has the amino acid sequence shown in SEQ ID NO: 6 or SEQ ID NO: 6 with conservative amino acid substitutions as claimed in amended independent claim 3. In order for a reference to be anticipatory, each and every element of the claimed invention must be found within the four corners of the cited reference. Rather simply does not teach or otherwise suggest the claimed nucleic acid molecule, and as such, is not an anticipatory reference. Thus, Rather et al. cannot anticipate the present claims.

In addition, Rather et al. do not teach or suggest a sequence that would be useful in the DOXP pathway. Rather et al. merely disclose a comparable sequence to gcpE in *E. coli* without explaining its function or suggesting the GcpE function. Moreover, Rather et al.'s sequence refers to an aarC gene that has the function of a negative regulator aac(2′)-la in *P. stuartii*. Therefore, Rather et al.'s sequence and the gcpE gene or the GcpE protein derived from *P. falciparum* are not functionally equivalent (*see, e.g.,* alleged functional equivalency between AarC and gcpE *E. coli*, which cannot be transformed into sequences of the present invention, at page 2272, left column).

In view of the above, Applicant submits that the claims as amended are not anticipated by Rather et al. and respectfully requests that this rejection be reconsidered and withdrawn.

CONCLUSION

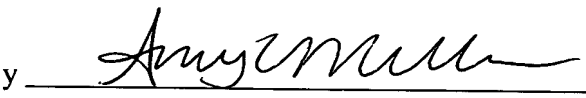
In light of the above, Applicant believes that this application is now in condition for allowance and therefore request favorable consideration.

If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 08-0750 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

HARNESS, DICKEY, & PIERCE, P.L.C.

By 

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